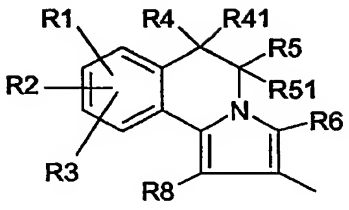
Patent claims

1. Use of a structure-element of the formula X



(X)

in which

in which

R1 is halogen, nitro, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxy-2-4C-alkoxy, 3-7C-cycloalkoxy or 3-7C-cycloalkylmethoxy,

R2 is 1-4C-alkoxy or halogen,

R3 is hydrogen or 1-4C-alkoxy,

R4 is hydrogen,

R41 is hydrogen,

R5 is hydrogen or 1-4C-alkyl, and

R51 is hydrogen or 1-4C-alkyl,

or

R4 is hydrogen,

R41 is hydrogen,

R5 is 1-4C-alkoxycarbonyl, and

R51 is hydrogen,

or

R4 is hydrogen,

R41 is hydrogen,

R5 is cyano, and

R51 is hydrogen,

or

R4 and R5 together form a 3-4C-alkylene bridge and R41 and R51 are both hydrogen,

R6 is 1-6C-alkyl, amino, formyl, or 1-4C-alkyl substituted by R61, in which

R61 is 1-4C-alkoxycarbonyl, carboxyl, 1-4C-alkoxy, hydroxyl, halogen or -N(R611)R612, in which

R611 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkyl-1-4C-alkyl, and

R612 is hydrogen or 1-4C-alkyl, or

R611 and R612 together and with inclusion of the nitrogen atom to which they are bound form a radical Het1, in which

Het1 is a 5- to 7-membered saturated heterocyclic ring radical comprising one nitrogen atom, to which R611 and R612 are bound, and, optionally, one further heteroatom selected from a group consisting of nitrogen, oxygen and sulfur, and optionally substituted by R613 on a ring nitrogen atom, in which

R613 is 1-4C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkyl-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl, amino-2-4C-alkyl, mono- or di-1-4C-alkylamino-2-4C-alkyl, formyl, pyridyl or pyrimidinyl,

R8 is cyano, or -C(O)-OR9, in which

R9 is 1-4C-alkyl;

under the provisio, that,

when R8 is -C(O)-OR9, in which

R9 is 1-4C-alkyl,

then R5 is other than hydrogen;

as integral part of the overall structure of compounds which inhibit PDE10.

2. Use of a structure-element of the formula X according to claim 1,

in which

R1 is halogen, nitro, 1-4C-alkyl, 1-4C-alkoxy, 1-4C-alkoxy-2-4C-alkoxy, 3-7C-cycloalkoxy or 3-7C-cycloalkylmethoxy,

R2 is 1-4C-alkoxy or halogen,

R3 is hydrogen or 1-4C-alkoxy,

R4 is hydrogen,

R41 is hydrogen,

R5 is hydrogen or 1-4C-alkyl, and

R51 is hydrogen or 1-4C-alkyl,

or

R4 is hydrogen,

R41 is hydrogen,

R5 is 1-4C-alkoxycarbonyl, and

R51 is hydrogen,

or

R4 and R5 together form a 3-4C-alkylene bridge and R41 and R51 are both hydrogen,

R6 is 1-6C-alkyl, amino, formyl, or 1-4C-alkyl substituted by R61, in which

R61 is 1-4C-alkoxycarbonyl, carboxyl, 1-4C-alkoxy, hydroxyl, halogen or -N(R611)R612, in which

R611 is hydrogen, 1-4C-alkyl, 3-7C-cycloalkyl or 3-7C-cycloalkyl-1-4C-alkyl, and

R612 is hydrogen or 1-4C-alkyl, or

R611 and R612 together and with inclusion of the nitrogen atom to which they are bound form a radical Het1, in which

Het1 is a 5- to 7-membered saturated heterocyclic ring radical comprising one nitrogen atom, to which R611 and R612 are bound, and, optionally, one further heteroatom selected from a group

consisting of nitrogen, oxygen and sulfur, and optionally substituted by R613 on a ring nitrogen atom,
in which

R613 is 1-4C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkyl-1-4C-alkyl, hydroxy-2-4C-alkyl, 1-4C-alkoxy-2-4C-alkyl, amino-2-4C-alkyl, mono- or di-1-4C-alkylamino-2-4C-alkyl, formyl, pyridyl or pyrimidinyl,

R8 is cyano, or -C(O)-OR9, in which

R9 is 1-4C-alkyl;

under the provisio, that,

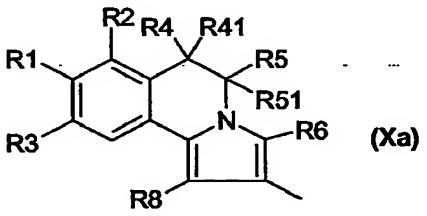
when R8 is -C(O)-OR9, in which

R9 is 1-4C-alkyl,

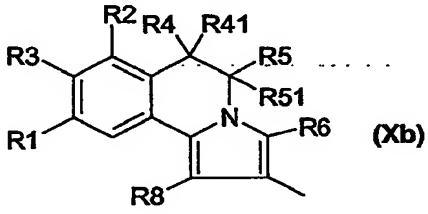
then R5 is other than hydrogen;

as integral part of the overall structure of compounds which inhibit PDE10.

3. Use according to claim 1, wherein said structure-element is of the formula Xa or Xb



(Xa)



(Xb)

in which

as a first alternative,

R1 is chlorine or fluorine,

R2 is hydrogen,

R3 is methoxy or ethoxy,

or, as a second alternative,

R1 is methoxy or ethoxy,

R2 is hydrogen,

R3 is methoxy or ethoxy,

or, as a third alternative,

R1 is chlorine or fluorine,

R2 is methoxy or ethoxy,

R3 is methoxy or ethoxy,

or, as a fourth alternative,

R1 is methoxy or ethoxy,

R2 is chlorine or fluorine,

R3 is methoxy or ethoxy,

or, as a fifth alternative,

R1 is methoxy or ethoxy,
R2 is methoxy or ethoxy,
R3 is methoxy or ethoxy,
R4 is hydrogen,
R41 is hydrogen,
R5 is methyl,
R51 is hydrogen,
R6 is methyl, ethyl or methoxycarbonylethyl,
R8 is cyano.

4. Use according to claim 1, wherein said structure-element is of the formula Xa as defined in claim 3, in which
R1 is methoxy,
R2 is hydrogen,
R3 is methoxy,
R4 is hydrogen,
R41 is hydrogen,
R5 is methyl,
R51 is hydrogen,
R6 is methyl or methoxycarbonylethyl,
R8 is cyano.

5. Use according to claim 1, wherein said structure-element is of the formula Xa or Xb as defined in claim 3,
in which
R1 is 1-2C-alkoxy,
R2 is hydrogen, chlorine or fluorine,
R3 is 1-2C-alkoxy,
R4 is hydrogen,
R41 is hydrogen,
R5 is hydrogen, 1-2C-alkyl or cyano,
R51 is hydrogen,
R6 is 1-2C-alkyl, or 1-2C-alkyl substituted by 1-2C-alkoxycarbonyl,
R8 is cyano.

6. Use according to claim 1, wherein said structure-element is of the formula Xa or Xb as defined in claim 3,
in which
R1 is 1-2C-alkoxy,
R2 is hydrogen, chlorine or fluorine,

R3 is 1-2C-alkoxy,

R4 is hydrogen,

R41 is hydrogen,

R5 is 1-2C-alkyl or cyano,

R51 is hydrogen,

R6 is 1-2C-alkyl, or 1-2C-alkyl substituted by 1-2C-alkoxycarbonyl,

R8 is -C(O)-OR9, in which

R9 is 1-2C-alkyl,

as integral part of the overall structure of compounds which inhibit PDE10.

7. Use according to claim 1, wherein said structure-element is selected from the group consisting of those structure-elements of the formula Xa as defined in claim 3,

in which

R1 is methoxy,

R3 is methoxy,

R4 is hydrogen,

R41 is hydrogen, and

R51 is hydrogen,

and in which the following combinations 1.) to 50.) of the substituent meanings for R2, R5, R6 and R8 apply:

	R2	R5	R6	R8
1.)	hydrogen	methyl	methyl	cyano
2.)	hydrogen	methyl	methyl	ethoxycarbonyl
3.)	hydrogen	methyl	2-methoxycarbonylethyl	cyano
4.)	hydrogen	methyl	2-methoxycarbonylethyl	ethoxycarbonyl
5.)	hydrogen	hydrogen	methyl	cyano
6.)	hydrogen	hydrogen	2-methoxycarbonylethyl	cyano
7.)	fluorine	methyl	methyl	cyano
8.)	fluorine	methyl	methyl	ethoxycarbonyl
9.)	fluorine	methyl	2-methoxycarbonylethyl	cyano
10.)	fluorine	methyl	2-methoxycarbonylethyl	ethoxycarbonyl
11.)	fluorine	hydrogen	methyl	cyano
12.)	fluorine	hydrogen	2-methoxycarbonylethyl	cyano
13.)	fluorine	hydrogen	methyl	ethoxycarbonyl
14.)	fluorine	hydrogen	2-methoxycarbonylethyl	ethoxycarbonyl
15.)	hydrogen	cyano	methyl	cyano
16.)	hydrogen	cyano	methyl	ethoxycarbonyl
17.)	hydrogen	cyano	2-methoxycarbonylethyl	cyano
18.)	hydrogen	cyano	2-methoxycarbonylethyl	ethoxycarbonyl
19.)	fluorine	cyano	methyl	cyano
20.)	fluorine	cyano	methyl	ethoxycarbonyl
21.)	fluorine	cyano	2-methoxycarbonylethyl	cyano
22.)	fluorine	cyano	2-methoxycarbonylethyl	ethoxycarbonyl
23.)	chlorine	methyl	methyl	cyano
24.)	chlorine	methyl	methyl	ethoxycarbonyl
25.)	chlorine	methyl	2-methoxycarbonylethyl	cyano
26.)	chlorine	methyl	2-methoxycarbonylethyl	ethoxycarbonyl
27.)	chlorine	hydrogen	methyl	cyano

28.)	chlorine	hydrogen	2-methoxycarbonylethyl	cyano
29.)	chlorine	hydrogen	methyl	ethoxycarbonyl
30.)	chlorine	hydrogen	2-methoxycarbonylethyl	ethoxycarbonyl
31.)	chlorine	cyano	methyl	cyano
32.)	chlorine	cyano	methyl	ethoxycarbonyl
33.)	chlorine	cyano	2-methoxycarbonylethyl	cyano
34.)	chlorine	cyano	2-methoxycarbonylethyl	ethoxycarbonyl
35.)	hydrogen	methyl	methyl	methoxycarbonyl
36.)	hydrogen	methyl	2-methoxycarbonylethyl	methoxycarbonyl
37.)	fluorine	methyl	methyl	methoxycarbonyl
38.)	fluorine	methyl	2-methoxycarbonylethyl	methoxycarbonyl
39.)	fluorine	hydrogen	methyl	methoxycarbonyl
40.)	fluorine	hydrogen	2-methoxycarbonylethyl	methoxycarbonyl
41.)	hydrogen	cyano	methyl	methoxycarbonyl
42.)	hydrogen	cyano	2-methoxycarbonylethyl	methoxycarbonyl
43.)	fluorine	cyano	methyl	methoxycarbonyl
44.)	fluorine	cyano	2-methoxycarbonylethyl	methoxycarbonyl
45.)	chlorine	methyl	methyl	methoxycarbonyl
46.)	chlorine	methyl	2-methoxycarbonylethyl	methoxycarbonyl
47.)	chlorine	hydrogen	methyl	methoxycarbonyl
48.)	chlorine	hydrogen	2-methoxycarbonylethyl	methoxycarbonyl
49.)	chlorine	cyano	methyl	methoxycarbonyl
50.)	chlorine	cyano	2-methoxycarbonylethyl	methoxycarbonyl

8. Use according to any of the preceding claims, wherein the compounds which inhibit PDE10 are used in therapy, such as, for example, in the treatment of neurologic and psychiatric disorders, such as e.g. anxiety or psychotic disorders, movement disorders, obsessive/compulsive disorders, drug addictions, cognition deficiency disorders, mood disorders or mood episodes, or neurodegenerative disorders; or in the treatment of diabetes; or in the regulation of fertility of men.

9. A method to inhibit PDE10 in the therapeutic treatment of a mammal, including human, such as e.g. in the treatment of neurologic and psychiatric disorders, in the treatment of diabetes, or in the regulation of fertility of a masculine mammal, comprising administering to said mammal a compound containing - as an integral part of its overall structure - a structure-element as defined in any of the claims 1 to 7.

10. A process to provide compounds, which inhibit PDE10, comprising the following steps:

a.) designing intellectually a structure of a compound comprising - as part of its overall structure - a structure-element as defined in any of the claims 1 to 7;

b.) synthesizing materially a compound, which have the structure designed in step a.), in a manner known to the person skilled in the art, or as disclosed in the specification of the present invention, or as disclosed in WO 02/48144, WO 03/014115, WO 03/014116 or WO 03/014117, or analogously or similarly thereto.

11. A process for providing PDE10 inhibitors of the pyrrolodihydroisoquinoline class comprising the following steps:

a.) selecting intellectually a structure of a compound of the pyrrolodihydroisoquinoline class;

b.) modifying intellectually said selected structure in such a way that the modified structure comprises - as part of its overall structure - a structure-element as defined in any of the claims 1 to 7;

c.) synthesizing materially a compound having said modified structure in a manner known to the person skilled in the art, or as disclosed in the specification of the present invention, or as disclosed in WO 02/48144, WO 03/014115, WO 03/014116 or WO 03/014117, or analogously or similarly thereto.

12. The process according to claim 11 comprising the following steps:

a.) selecting intellectually a structure of a compound disclosed in WO 02/48144, WO 03/014115, WO 03/014116, WO 03/014117 or WO 03/051877, such as, for example,
a structure of a compound mentioned expressis verbis or individualized by way of example therein, or a structure of a compound emphasized therein and/or a structure of a compound disclosed therein with advantageous effects, such as e.g. advantageous PDE10 inhibiting values;

b.) modifying intellectually said selected structure in such a way that the modified structure comprises - as part of its overall structure - a structure-element as defined in any of the claims 1 to 7;

c.) synthesizing materially a compound having said modified structure in a manner known to the person skilled in the art, or as disclosed in the specification of the present invention, or as disclosed in WO 02/48144, WO 03/014115, WO 03/014116, WO 03/014117 or WO 03/051877, or analogously or similarly thereto.

13. A compound obtainable by the process according to any of the claims 10 to 12.

14. A method for treating disorders of the central nervous system, such as, for example, anxiety or psychotic disorders, such as e.g. schizophrenia, movement disorders, obsessive/compulsive disorders, drug addictions, cognition deficiency disorders, mood disorders or mood episodes, or neurodegenerative disorders, by inhibiting of PDE10 comprising administering to a subject in need thereof a pharmaceutically effective and tolerable amount of a compound obtainable by a process according to any of the claims 9 to 11.

15. A compound, which inhibits PDE10 and which comprises a structure-element according to any of the claims 1 to 7 as an integral part of its overall structure.